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LETTER TO THE EDITOR

Response to letter by A. García Arieta

I thank Dr Arieta for his comment to the paper ''Lung function and asthma control with beclomethasone and formoterol in a single inhaler'' published on the January issue of this Journal.[1]

He suggests that the superiority in some parameters of asthma control achieved with beclomethasone (BDP)/formoterol (FF) extrafine HFA fixed combination over BDP CFC and FF DPI given via separate inhalers is due to the extrafine nature of BDP in the fixed combination, rather than to the co-deposition of BDP and FF in the lung allowed by the co-administration of the active principles in a single inhaler.

We agree that this explanation is in line both with the pharmacokinetics data reported with the extrafine BDP/FF combination[2] and with previous evidence of superiority of BDP extrafine versus BDP CFC in clinical parameters different from lung function.[3,4] This confirms the importance to have an extrafine formulation able to achieve high lung deposition and homogeneous distribution throughout the lung, including the small airways.

However, we believe that, based on the current knowledge, the explanation of this interesting and novel finding for an ICS/LABA combination might be more complex. The synergistic effect of LABA and ICS is well documented at various cellular levels, both in the central and in the peripheral bronchial tree.[5–8] When formulated as extrafine, ICS and LABA are expected to be efficiently and homogeneously co-deposited in all the districts of the lungs, as already shown *in vitro* with the extrafine HFA BDP/FF combination under investigation.[9] Our hypothesis is therefore that the extrafine formulation not only favours the efficient lung deposition of BDP and its peripheral distribution, as stated by Dr Arieta, but also allows the efficient co-deposition of both the BDP and FF throughout the lung, thus enabling the synergistic effect of the two drugs in all the districts of the bronchial tree. Overall, this would contribute to the clinical superiority observed in this study over the separate, nonextrafine components, which has never been reported for other nonextrafine ICS/LABA fixed combinations.

The results of the study performed do not allow to discriminate the separate contribution of the extrafine formulation and the improved co-deposition due to the single inhaler administration, therefore we hypothesised that both features might concur in the beneficial effect on asthma control observed with the extrafine BDP/FF combination compared to nonextrafine BDP plus FF administered as separate components.

Whether the property of ICS and LABA co-deposition and its clinical benefit is attributable mainly to fixed combinations rather than to free combinations, as suggested by some authoritative investigators,[10] should be definitively demonstrated in a properly designed clinical trial.

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Jean Bousquet
Clinique des Maladies Respiratoires, Hôpital Arnaud de Villeneuve, Centre Hospitalier Universitaire, Cedex 5, 34295 Montpellier, France

E-mail address: jean.bousquet@orange.fr

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